REMARKS/ARGUMENTS

Upon entry of this amendment, claims 24-29 are pending in this application and are presented for examination. Claims 24-26 have been amended. No new matter has been introduced with the foregoing amendments. Reconsideration is respectfully requested.

I. FORMALITIES

Applicants thank the Examiner for the telephone interview of August 5, 2004. At the Examiner's request, Applicants provide below a detailed description of Figure 15. A copy of Figure 15 is attached herewith for the Examiner's convenience.

Claims 24-26 have been amended. Support for amended claim 24 is found throughout the specification as filed, *e.g.*, in Example 4 on pages 28-30 and in Figure 15. Claim 24 has also been amended to delete the phrase "wherein contacting said retrovirus with said compound inactivates said retrovirus" to eliminate redundancy within the claim. Claim 25 has been amended to correct the spelling of "Tetraethylthiuram." Claim 26 has been amended to include a verb in the sentence. Thus, no new matter has been introduced. As such, Applicants respectfully request that the amendments to the claims be entered.

II. REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claim 26 was rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. To the extent the rejection is applicable to the amended set of claims, Applicants respectfully traverse the rejection.

The Examiner alleges that because claim 24 excludes the disulfide compound 5,5-Dithiobis(2-Nitrobenzoic Acid) ("DTNB") but claim 26 does not, it is unclear which disulfide compounds are intended to be excluded from claim 26. For the reasons set forth below, Applicants have amended claim 24 to delete the proviso excluding DTNB. As a result, there is no discrepancy between the disulfide compounds claimed in claim 26 and amended claim 24. Thus, Applicants respectfully request that the Examiner withdraw the 35 U.S.C. § 112, second paragraph, rejection.

III. REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 24-29 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the Applicants, at the time the application was filed, had possession of the claimed invention. To the extent the rejection is applicable to the amended set of claims, Applicants respectfully traverse the rejection.

The Examiner alleges that the specific exclusion of DTNB from the claims constitutes new matter. In order to expedite prosecution of the present case, Applicants have amended claim 24 to delete the proviso excluding DTNB and to recite a composition comprising an inactivated ***intact*** retrovirus, wherein the ***intact*** retrovirus is inactivated due to disruption of one or more CCHC zinc fingers in a nucleocapsid ("NC") protein by contact with one of the compounds recited therein. Consequently, any disulfide compound that has no effect on inactivating an ***intact*** retrovirus (*e.g.*, DTNB) falls outside the scope of claim 24 as amended.

Further, Applicants submit herewith a Declaration of Dr. Louis E. Henderson under 37 C.F.R. § 1.132 ("the Declaration"). As explained by Dr. Henderson in the Declaration, the instant specification describes a specific set of tests for readily determining whether a disulfide compound of interest is capable of inactivating an ***intact*** retrovirus by disrupting NC zinc fingers. Again, any disulfide compound such as DTNB that has no effect on inactivating an ***intact*** retrovirus simply falls outside the scope of claim 24 as amended.

As set forth by Dr. Henderson in the Declaration, Example 4 of the instant specification describes a first test in which a disulfide compound of interest is incubated with ***purified, recombinant*** NC protein and the ability of the disulfide compound to oxidize, *i.e.*, disrupt, the CCHC zinc fingers in the NC protein is determined by monitoring the formation of NC cross-links (*see,* page 29, lines 4-17). In particular, the results shown in Table 2 under "Protein (HPLC)" indicate that a wide variety of the 43 disulfide compounds tested disrupt the CCHC zinc fingers in ***purified, recombinant*** NC protein. As such, this test provides a simple initial screen to identify candidate disulfide compounds with NC cross-linking activity. However, this test does not indicate whether disulfide compounds capable of cross-linking

purified, recombinant NC protein will also be effective at inactivating ***intact*** retroviruses. To this end, Example 4 also describes a second test in which the disulfide compound of interest is incubated with ***intact*** retroviruses (*see,* page 29, line 18 to page 30, line 20). The ability of the disulfide compound to inactivate ***intact*** retroviruses, *i.e.,* by penetrating the viral envelope and disrupting NC protein structure, is determined, for example, by: (1) visualizing the formation of NC multimers using Western blot analysis (*e.g.,* Figure 15A); (2) measuring the time required to cross-link half of the NC protein (*e.g.,* Table 2 under "X-link T-½ (min)"); and (3) measuring the concentration of the disulfide compound required to inactivate half of a standardized number of ***intact*** retroviruses in a tissue culture infectivity assay (*e.g.,* Figure 15B).

For example, Dr. Henderson points out in the Declaration that Figure 15A shows the NC cross-linking activity of 12 disulfide compounds on ***intact*** HIV-1 retroviruses, in which ***intact*** HIV-1 retroviruses alone ("HIV-1," lane 1) and those exposed to N-ethylmaleimide ("NEM," lane 2) were used as controls. Strikingly, the appearance of NC multimers and/or the disappearance of NC monomers, dimers, trimers, and tetramers was associated with exposure of ***intact*** HIV-1 retroviruses to each of the 9 disulfide compounds listed in lanes 6-14, indicating that these disulfide compounds are highly effective at penetrating the viral envelope and disrupting NC protein structure in ***intact*** HIV-1 retroviruses. By contrast, NC protein structure in ***intact*** HIV-1 retroviruses exposed to DTNB (lane 5) was nearly indistinguishable from controls. Although DTNB has excellent NC cross-linking activity on ***purified, recombinant*** NC protein (*see,* Table 2 on page 33), it is membrane-impermeant and therefore cannot penetrate the viral envelope to reach and disrupt NC protein structure in ***intact*** HIV-1 retroviruses. Similarly, NC protein structure in ***intact*** HIV-1 retroviruses exposed to 4-(Dimethylamino)phenyl Disulfide ("B2d," lane 3) or Benzoyl Disulfide ("A3c," lane 4) was also nearly indistinguishable from controls. However, unlike DTNB, B2d and A3c are membrane-permeant, but have poor NC cross-linking activity. As a result, in this test, the amount of NC multimers formed were below the limit of detection.

As further explained by Dr. Henderson in the Declaration, the graph in Figure 15B[1] extends the findings of Figure 15A by showing the association between viral envelope

penetration and NC cross-linking activity on the inactivation of ***intact*** HIV-1 retroviruses in a tissue culture infectivity assay. In particular, the highly effective ability of C4b, C1d, and D1b to penetrate the viral envelope and disrupt NC protein structure in ***intact*** HIV-1 retroviruses (*see,* Figure 15A, lanes 6-8) was associated with the ability of increasing concentrations of C4b (open diamond), C1d (filled square), and D1b (filled circle) to inactivate ***intact*** HIV-1 retroviruses. By contrast, the inability of DTNB to penetrate the viral envelope in ***intact*** HIV-1 retroviruses (*see,* Figure 15A, lane 5) was associated with the inability of DTNB (open circle with dashed line) to inactivate ***intact*** HIV-1 retroviruses, even at the highest concentration tested. The poor ability of membrane-permeant B2d and A3c to disrupt NC protein structure in ***intact*** HIV-1 retroviruses (*see,* Figure 15A, lanes 3-4) was associated with the need for higher concentrations of B2d (filled diamond) and A3c (open square) to inactivate ***intact*** HIV-1 retroviruses. As such, these results show that membrane-permeant disulfide compounds with either poor (*e.g.,* B2d, A3c) or excellent (*e.g.,* C4b, C1d, D1b) NC cross-linking activity were able to inactivate ***intact*** HIV-1 retroviruses, while membrane-impermeant disulfide compounds, even with excellent NC cross-linking activity (*e.g.,* DTNB), had no effect.

Similarly, Dr. Henderson points out in the Declaration that the graph in Figure 15B[2] extends the findings of Figure 15A by showing that the highly effective ability of FDA, E4b, E1b, C3d, and C4d to penetrate the viral envelope and disrupt NC protein structure in ***intact*** HIV-1 retroviruses (*see,* Figure 15A, lanes 10-14) was associated with the ability of increasing concentrations of FDA (filled circle), E4b (filled square), E1b (open triangle), C3d (open circle), and C4d (open square) to inactivate ***intact*** HIV-1 retroviruses. By contrast, the reduced monomeric form of FDA ("Mon," filled square with dashed line) had no effect on inactivating ***intact*** HIV-1 retroviruses. As such, these results show that membrane-permeant disulfide compounds with excellent NC cross-linking activity (*e.g.,* FDA, E4b, E1b, C3d, C4d) were able to inactivate ***intact*** HIV-1 retroviruses, while reduced monomeric forms of these disulfide compounds with no NC cross-linking activity (*e.g.,* Mon) had no effect.

In view of the foregoing, Applicants believe that the specification describes a specific set of tests for readily determining whether a disulfide compound of interest is capable

of inactivating an ***intact*** retrovirus by disrupting NC zinc fingers. As a result, Applicants assert that amended claim 24 by definition excludes any NC zinc finger-disrupting compound such as DTNB that has no effect on inactivating an ***intact*** retrovirus because any such compound would simply fall outside the scope of the claim. Therefore, Applicants respectfully request that the Examiner withdraw the 35 U.S.C. § 112, first paragraph, rejection.

IV. DOUBLE PATENTING REJECTION

Claims 24-29 were rejected under the judicially created doctrine of obviousness-type double patenting for allegedly not being patentably distinct over claims 1, 6-9, and 25-28 of U.S. Patent No. 6,001,555. In the Office Action, the Examiner has indicated that the double patenting rejection can be overcome by the filing of a Terminal Disclaimer (*see*, page 5 of the Office Action).

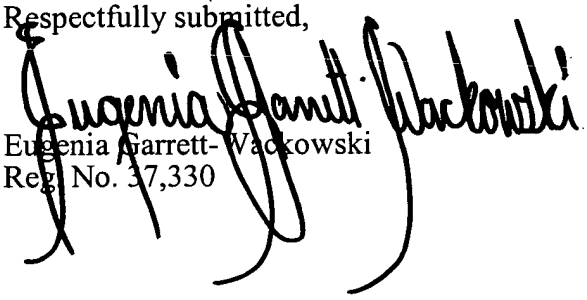
Applicants respectfully request that this obviousness-double patenting rejection be held in abeyance until Applicants receive from the Examiner an indication regarding allowable subject matter. At that time, Applicants will file a Terminal Disclaimer as suggested by the Examiner.

V. CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



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